REMARKS

Claims 1, 19, 21, 24-27, 30-32 and 34-63 are pending. Claims 1, 19, 21, 24-27, 30-32 and 34-36 stand rejected, and claims 37-63 are withdrawn. In this Amendment, claims 1, 19, 21, 24, 30-32, 35, and 36 are amended, and claims 25-27 and 34 are canceled. Reconsideration is respectfully requested.

New Dependent Claims

Amended claims 1, 35, and 36 incorporate elements from canceled claims 25-27. Moreover, amended claims 1, 19, 21, 24, 30-32, 35, and 36 do not require the non-cross-linked polymeric material and hence are similar to the claims as previously pending prior to the Amendment filed February 25, 2010. No new matter is introduced.

The First Rejection Under 35 U.S.C. § 103(a) Is Traversed

Claims 1, 19, 21, 24-25, 29, 31, 34, and 36 are rejected under 35 U.S.C. § 103 as being allegedly obvious over U.S. 4,482,386 ["*Wittwer*"], U.S. 5,135,755 to ["*Czech*"], and further in view of any one of JP 05308969 ("'969") or JP Laid-open Publication No. 6-254148 ("'148") discussed in the English translation of the Official Japanese Action in JP Patent Application No. 2001-502866 ("'866"). Applicants respectfully traverse.

According to MPEP § 2143, to support a *prima facie* case of obviousness it is important to identify a reason that would have prompted the artisan to combine the elements in the way the presently claimed new invention does. Moreover, all claim elements must be considered and shown to be present when determining patentability against the cited references.

Independent Claim 1

Amended claim 1 recites a biocompatible, resorbable, single-phase aqueous colloid, which is substantially free from a free aqueous phase. The colloid is present in an applicator having an extrusion orifice, has been fragmented by mechanical disruption, comprises a cross-linked gelatin polymer present in discrete subunits, has an equilibrium swell from 400% to 5000%, and has at least one characteristic selected from the group consisting of (a) a subunit size when fully hydrated in the range from 0.01 mm to 5 mm, and (b) an *in vivo* degradation time

of less than one year. Additionally, the single phase aqueous colloid is at least partially hydrated with an aqueous medium, and the aqueous medium includes an active clotting agent that is thrombin.

Office Action Does Not Address Equilibrium Swell From 400% to 5000%

Claim 1 includes the recitation that the single-phase aqueous colloid has an equilibrium swell from 400% to 5000%. Although *Wittwer* discusses "swellable" hydrocolloids, the Office Action does not address where any of the cited references teach or suggest an equilibrium swell from 400% to 5000%.

Office Action Does Not Address Substantially Free of Free Aqueous Phase

Claim 1 also includes the recitation that the single-phase aqueous colloid is substantially free from a free aqueous phase. The current application at paragraph [0022] describes this phrase in some embodiments as meaning fully or partially hydrated, but not hydrated above their capacity to absorb water. The Office Action, however, has not addressed where any of the references makes such a teaching or suggestion with regard to claim 1.

Wittwer Does Not Show Fully Hydrated Subunit Size of 0.01 to 5 mm

The Office cites *Wittwer* for describing hydrocolloids with subunits in the range from 0.01 mm to 5 mm. Although claim 6 of *Wittwer* discusses particle sizes of 0.2 to 4 mm, with regard to hydration, col. 4 lines 46-48 describe only a 2 mm gelatin granule having a water content of 15% b.w. There is no discussion in *Wittwer* of a fully hydrated granule. To the contrary, *Witter* at col. 3 ln. 15 *et seq.* reports that the feeding process should use devices suitable for "powdery material."

As noted above, current claim 1 recites "a subunit size when fully hydrated in the range from 0.01 mm to 5 mm[.]" At paragraph [0025] of the current Application, the term dry is used to describe compositions with moisture contents of below 20% by weight of water. That same paragraph goes on to describe hydrated as above 50%, and in some embodiments to be in the range of from 75% to 95% by weight of water.

Based on the above, *Wittwer* does not teach a fully hydrated subunit size of 0.01 to 5 mm as recited in claim 1.

Office Action Is Conclusory Regarding *In Vivo* Degradation

The Office Action states at page 3 that "the property of degradation is associated with gelatin." This conclusion is not sufficient to show that any of the references teach or suggest an *in vivo* degradation time of less than one year, as recited in claim 1. Moreover, *Wittwer* seeks "to avoid chemical and mechanical degradation," as stated at col. 1, ll. 62-63. The industrial process discussed in *Wittwer* provides no suggestion that injection molded products are intended to degrade *in vivo* in any time frame. Hence, the references do not teach or suggest an *in vivo* degradation time of less than one year, but expressly seek to avoid such an outcome. According to MPEP 2141.02, a cited reference must be considered in its entirety, i.e. as a whole, including portions that teach or lead away from the claimed invention. Accordingly, it is improper to ignore *Wittwer* to the extent it teaches away from degradation.

JP '148 is Irrelevant, and an Invalid Reference as it is Currently Being Asserted

According to the Office Action, the JP '148 reference describes the combination of cross-linked and non-cross-linked gelatin for a hemostatic application. As noted above, the amended independent claims do not require the non-cross-linked gelatin. Hence, JP '148 is not relevant to the pending claims.

Regardless, the available English abstract of the JP '148 reference discusses gelatin attached to a nonwoven fabric. In no way does this teach or suggest a combination of cross-linked and non-cross-linked gelatins as recited in the current claims.

The Office has asserted that "according to the description given the translation" the reference indeed makes such a teaching. However, the translation provided is not of the JP '148 reference, but of an Office Action provided by the Japanese Patent Office. This is not an appropriate reference as stated by the MPEP.

MPEP § 901.05 states that, "All foreign patents, published applications, and any other published derivative material containing portions or summaries of the contents of published or unpublished patents (e.g. abstracts). . . are available to U.S. examiners." This list does not include characterizations by foreign examiners. Moreover, MPEP § 706.02(II) states that, "When an abstract is used to support a rejection, the evidence relied upon is the facts contained in the abstract, not additional facts that may be contained in the underlying full text document." That section goes on to state that

> To determine whether both the abstract and the underlying document are prior art, a copy of the underlying document must be obtained and analyzed. If the document is in a language other than English and the examiner seeks to rely on that document, a translation must be obtained so that the record is clear as to the precise facts the examiner is relying upon in support of the rejection.

Applicants therefore request the withdrawal of the rejection over the JP '148 reference absent a showing that the underlying document in fact describes what the foreign examiner alleges that it describes, supported by a translation to clarify the record, as required by MPEP 706.02(II), and a showing that the Japanese Office Action, which published Dec. 24, 2009, may properly be relied upon under MPEP § 706.02(II), § 901.05, or any other rule or regulation.

Czech Is Irrelevant, and Uses Cross-Linked Gelatin Only

As noted above, the amended independent claims do not require the non-cross-linked gelatin. Hence, *Czech* is not relevant to the pending claims.

Regardless, the actual product discussed in *Czech* does not contain both cross-linked and non-cross-linked gelatins, but only cross-linked components. Moreover, *Czech* states at col. 1, ll. 62-66, that certain attributes (e.g. mechanical strength, stability, and transparency) are obtained by cross-linking biopolymers and synthetic polymers together.

No Motivation to Combine *Wittwer* with JP '969

The Office Action states that it would be obvious to incorporate the materials of the JP '969 reference with the molding techniques of *Wittwer*. Applicants cannot agree.

Wittwer discusses a high-temperature industrial process for preparing hydrocolloids for injection molding. *Wittwer* includes processing the gelatin through a tube to reach a discharge temperature of 100°C (212°F). It is well known, however, that enzymes typically become denatured and lose their activity when subjected to boiling temperatures. Hence, there is no indication that the enzyme composition described in the JP '969 reference would be able to survive *Wittwer's* process which occurs at the boiling point of water. Similarly, one of skill in the art in producing JP '969's enzyme composition would not be motivated to use *Wittwer's* high temperature industrial injection molding processes in an attempt to produce a composition as recited in claim 1, particularly one that includes thrombin as an active clotting

agent. This discussion of the patentability of the cross-linked gelatin and thrombin combination is also relevant to the second §103 Rejection, presented below.

For at least the reasons provided above, Applicants submit that the sum of the cited references does not teach or suggest the presently claimed combination of elements as recited in independent claim 1. Furthermore, there is no identifiable proper reason that would have prompted the skilled artisan to combine the elements as recited in claim 1. Hence, the proposed combination does not meet the requirements of a *prima facie* case of obviousness.

Because of the deficiencies of the cited references, the limitations not taught by the cited references, as well as the lack of a proper motivation to combine the references, amended independent claim 1 is believed allowable over the cited references. Accordingly, withdrawal of the § 103 rejection is respectfully requested.

Claims 19, 21, 24-25, 29 and 31

Each of claims 19, 21, 24-25, 29 and 31 depend, either directly or indirectly from claim 1, and are believed allowable over the cited references due at least to their dependence on an allowable base claim. As such, Applicants respectfully request withdrawal of the rejections of these claims.

Independent Claim 36

Independent claim 36 recites elements similar to those described in claim 1. Claim 36 is rejected over the same references as applied to claim 1, and the remarks applying to claim 1 are similarly applicable to claim 36. Accordingly, claim 36 is believed allowable over the cited references for at least the reasons discussed previously.

The Second Rejection Under § 103 is Traversed

As noted above, elements of canceled claims 26 and 27 are now incorporated into the amended independent claims.

Claims 26 and 27 are rejected as being allegedly obvious over the references as applied to claim 1, in further view of U.S. Patent No. 5,643,596 to *Pruss et al.*, and/or U.S. Patent No. 4,515,637 to *Cioca*. Applicants respectfully traverse.

Pruss is cited for describing a hemostatic patch comprising clot promoting amounts of thrombin, and *Cioca* is cited for describing thrombin as an effective clotting factor. Yet neither of these references remedy the deficiencies of *Wittwer*, *Czech*, and JP '148, which were cited against claim 1.

Moreover, as noted above, the artisan would have no rational reason to use *Wittwer's* high-temperature injection molding industrial processes for preparing compositions containing thrombin. It is well known that enzymes typically become denatured and lose their activity when subjected to boiling temperatures, and there is no indication that the thrombin described in *Pruss* or *Cioca* would be able to survive *Wittwer's* process which occurs at the boiling point of water. Accordingly, one of skill in the art in producing *Pruss* or *Cioca's* thrombin would not be motivated to use *Wittwer's* high temperature industrial injection molding processes in an attempt to produce a composition as recited in claim 1, particularly one that includes thrombin as an active clotting agent.

Based on the above, Applicants respectfully request the withdrawal of the § 103 rejection.

The Third Rejection Under § 103 is Traversed

Claims 30 and 35 are rejected as being allegedly obvious over the references as applied to claim 1, in further view of U.S. Patent No. 4,124,705 to *Rothman et al.*, or the combination of *Rothman* and U.S. Patent No. 6,129,761 to *Hubbell*. Applicants respectfully traverse.

Rothman is cited for describing an agent for intravascular administration consisting of a suspension of particles of a polysaccharide, and *Hubbell* is cited for describing injectable compositions including polysaccharides. However, again these references do not remedy the deficiencies of *Wittwer*, *Czech*, and JP '148, which were cited against claim 1. Claim 30 indirectly depends from claim 1, and is believed allowable at least by virtue of its dependence from an allowable base claim. The references as applied to claim 1 are deficient with regard to claim 35 for each of the reasons stated with regard to claim 1, and the remarks presented previously are applicable to claim 35 as well.

Additionally, under either scenario of the current rejection, the Office relies on *Rothman* to teach the composition containing the polysaccharide. The Office Action states at page 8 that, with respect to the recitations of the combination composition being single phase and substantially free from a free aqueous phase, *Rothman* does not include any other substance or component in the polysaccharide suspension. However, this statement includes the inherent flaw in applying *Rothman* to claim 35: In *Rothman* the polysaccharide is in aqueous suspension, which is by nature a free aqueous phase. Col. 9, ll. 49-62, of *Rothman* describes the free aqueous phases that can be used to suspend the polysaccharide particles prior to intravenous injection. Furthermore, col. 9, ll. 63-65, state that, "An agent or composition according to the invention is prepared by suspending the particles described above in a physiologically acceptable aqueous liquid."

Finally, as would be known by one of skill in the art, a suspension can be considered a multi-phase heterogeneous mixture. In fact, at col. 2, ll. 4-6, *Rothman* states that the polysaccharide agent is water-insoluble, and thus is incapable of creating a homogenous, single-phase solution. Consequently, it cannot be maintained that *Rothman* teaches a composition that is either single phase or substantially free from a free aqueous phase. Therefore, combining the teachings of *Rothman* with the other cited references directly contravenes the recitations of claims 30 and 35, and one of skill in the art would not combine the cited references to produce a single phase combined composition that is substantially free from a free aqueous phase.

For at least these reasons, claims 30 and 35 are believed allowable over the prior art references. Accordingly, withdrawal of the § 103 rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,

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